

S/N Unknown

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	David Wiemer et al.	Examiner:	Unknown
Serial No.:	Unknown	Group Art Unit:	Unknown
Filed:	Herewith	Docket:	875.050US2
Title:	ISOPRENOID ANALOG COMPOUNDS AND METHODS OF MAKING AND USE THEREOF		
	(Divisional of U.S. Serial No. 10/116,737 filed April 3, 2002)		

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

In compliance with the duty imposed by 37 C.F.R. § 1.56, and in accordance with 37 C.F.R. §§ 1.97 *et. seq.*, the enclosed materials are brought to the attention of the Examiner for consideration in connection with the above-identified patent application. Applicants respectfully request that this Information Disclosure Statement be entered and the documents listed on the attached Form 1449 be considered by the Examiner and made of record. Pursuant to the provisions of MPEP 609, Applicants request that a copy of the 1449 form, initialed as being considered by the Examiner, be returned to the Applicants with the next official communication.

Pursuant to 37 C.F.R. §1.97(b), it is believed that no fee or statement is required with the Information Disclosure Statement. However, if an Office Action on the merits has been mailed, the Commissioner is hereby authorized to charge the required fees to Deposit Account No. 19-0743 in order to have this Information Disclosure Statement considered.

Pursuant to 37 C.F.R. §1.98(d), copies of the listed documents are not provided as these references were previously cited by or submitted to the U.S. Patent Office in connection with Applicants' prior U.S. application, Serial No. 10/116737, filed on April 03, 2002, which is relied upon for an earlier filing date under 35 U.S.C. §120.

INFORMATION DISCLOSURE STATEMENT

Serial No :Unknown

Filing Date: Herewith

Title: ISOPRENOID ANALOG COMPOUNDS AND METHODS OF MAKING AND USE THEREOF

Page 2

Dkt: 875.050US2

The Examiner is invited to contact the Applicants' Representative at the below-listed telephone number if there are any questions regarding this communication.

Respectfully submitted,

DAVID WIEMER ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 359-3265

Date Feb. 17, 2004

By Nicole N. Morris
Nicole N. Morris
Reg. No. P-55,467

"Express Mail" mailing label number: EV 299 686 741 US

Date of Deposit: February 17, 2004

This paper or fee is being deposited on the date indicated above with the United States Postal Service pursuant to 37 CFR 1.10, and is addressed to the Commissioner for Patents, Mail Stop Patent Application, P.O. Box 1450, Alexandria, VA 22313-1450.

Substitute for form 1449A/PTO
**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**
(Use as many sheets as necessary)

Complete if Known

Application Number	Unknown
Filing Date	Even Date Herewith
First Named Inventor	Wiemer, David
Group Art Unit	Unknown
Examiner Name	Unknown

Sheet 1 of 5

Attorney Docket No: 875.050US2

US PATENT DOCUMENTS

Examiner Initial *	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	Filing Date If Appropriate
	US-5,574,025	11/12/1996	Anthony, N J., et al.	514	129	10/26/1994

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	T ²
--------------------	---------------------	------------------	---	-------	----------	----------------

OTHER DOCUMENTS -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		ADJEI, A A., et al., "A Phase I Trial of the Farnesyl Transferase Inhibitor SCH66336: Evidence for Biological and Clinical Activity", <u>Cancer Research</u> , Vol. 60,(April 1, 2000),pp. 1871-1877	
		ASHAR, H R., et al., "Farnesyl Transferase Inhibitors Block the Farnesylation of CENP-E and CENP-F and Alter the Association of CENP-E with the Microtubules", <u>The Journal of Biological Chemistry</u> , Vol. 275, No. 39,(September 29, 2000),pp. 30451-30457	
		BERGO, M O., et al., "Targeted Inactivation of the Isoprenylcysteine Carboxyl Methyltransferase Gene Causes Mislocalization of K-Ras in Mammalian Cells", <u>The Journal of Biological Chemistry</u> , Vol. 275, No. 23,(2000),pp. 17605-17610	
		CASEY, P J., et al., "Enzymatic modification of proteins with a geranylgeranyl isoprenoid", <u>Proc. Natl. Acad. Sci. USA</u> , Vol. 88,(October, 1991),pp. 8631-8635	
		CERMAK, D M., et al., "2-(Acyloxy)ethylphosphonate Analogues of Prenyl Pyrophosphates: Synthesis and Biological Characterization", <u>Bioorganic & Medicinal Chemistry</u> , Vol. 8,(2000),2729-2737	
		CERMAK, D M., et al., "Synthesis of Nonracemic Dimethyl Alpha-(Hydroxyfarnesyl)phosphonates via Oxidation of Dimethyl Farnesylphosphonate with (Camphorsulfonyl)oxaziridines", <u>J. Org. Chem.</u> , Vol. 64, No. 2,(1999),pp. 388-393	
		CHANG, JEN-WEN A., et al., "Stereoelectronic Effects on the Conformation and Kinetics of Nucleophilic Displacement Reactions in Epimeric Six-membered Ring Phosphonate Diesters", <u>Tetrahedron</u> , Vol. 43, No. 22,(1987),pp. 5187-5196	
		CHEHADE, K A., et al., "Design and Synthesis of a Transferable Farnesyl Pyrophosphate Analogue to Ras by Protein Farnesyltransferase", <u>J. Org. Chem.</u> , Vol. 65, No. 10,(2000),pp. 3027-3033	

EXAMINER

DATE CONSIDERED

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

Substitute for form 1449A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td colspan="2" style="padding: 2px;"><i>Complete if Known</i></td> </tr> <tr> <td style="width: 60%; padding: 2px;">Application Number</td> <td style="padding: 2px;">Unknown</td> </tr> <tr> <td style="padding: 2px;">Filing Date</td> <td style="padding: 2px;">Even Date Herewith</td> </tr> <tr> <td style="padding: 2px;">First Named Inventor</td> <td style="padding: 2px;">Wiemer, David</td> </tr> <tr> <td style="padding: 2px;">Group Art Unit</td> <td style="padding: 2px;">Unknown</td> </tr> <tr> <td style="padding: 2px;">Examiner Name</td> <td style="padding: 2px;">Unknown</td> </tr> </table>	<i>Complete if Known</i>		Application Number	Unknown	Filing Date	Even Date Herewith	First Named Inventor	Wiemer, David	Group Art Unit	Unknown	Examiner Name	Unknown
<i>Complete if Known</i>													
Application Number	Unknown												
Filing Date	Even Date Herewith												
First Named Inventor	Wiemer, David												
Group Art Unit	Unknown												
Examiner Name	Unknown												
Sheet 2 of 5	Attorney Docket No: 875.050US2												

		CHEN, Z , et al., "Both Farnesylated and Geranylgeranylated RhoB Inhibit Malignant Transformation and Suppress Human Tumor Growth in Nude Mice", <u>The Journal of Biological Chemistry</u> , Vol. 275, No. 24,(June 16, 2000),pp. 17974-17978	
		DAVISSON, V J., et al., "Phosphorylation of Isoprenoid Alcohols", <u>J. Org. Chem.</u> , Vol. 51, No. 25,(1986),pp. 4768-4779	
		DING, C Z., et al., "Discovery and Structure-Activity Relationships of Imidazole-Containing Tetrahydrobenzodiazepine Inhibitors of Farnesyltransferase", <u>J. Med. Chem.</u> , Vol. 42, No. 25,(1999),pp. 5241-5253	
		DU, W , et al., "Geranylgeranylated RhoB Mediates Suppression of Human Tumor Cell Growth by Farnesyltransferase Inhibitors", <u>Cancer Research</u> , Vol. 59,(November 1, 1999),pp. 5492-5496	
		EDAMATSU, H , et al., "Cdk inhibitors, roscovitine and olomoucine, synergize with farnesyltransferase inhibitor (FTI) to induce efficient apoptosis of human cancer cell lines", <u>Oncogene</u> , Vol. 19,(2000),pp. 3059-3068	
		EDELSTEIN, R L., et al., "Stereochemical Analysis of the Reaction Catalyzed by Yeast Protein Farnesyltransferase", <u>J. Org. Chem.</u> , Vol. 63, No. 16,(1998),pp. 5298-5299	
		FINDER, J D., et al., "Inhibition of Protein Geranylgeranylation Causes a Superinduction of Nitric-oxide Synthase-2 by Interleukin-1Beta in Vascular Smooth Muscle Cells", <u>The Journal of Biological Chemistry</u> , Vol. 272, No. 21,(May 23, 1997),pp. 13484-13488	
		FLINT, O R., et al., "HMG CoA Reductase Inhibitor-Induced Myotoxicity: Pravastatin and Lovastatin Inhibit the Geranylgeranylation of Low-Molecular-Weight Proteins in Neonatal Rat Muscle Cell Culture", <u>Toxicology and Applied Pharmacology</u> , Vol. 145,(1997),pp. 99-110	
		GALBIATI, F , et al., "The Dually Acylated NH2-terminal Domain of Gi1Alpha Is Sufficient to Target a Green Fluorescent Protein Reporter to Caveolin-enriched Plasma Membrane Domains", <u>the Journal of Biological Chemistry</u> , Vol. 274, No. 9,(February 26, 1999),pp. 5843-5850	
		GAON, I , "Photoactive Analogs of Farnesyl Pyrophosphate Containing Benzoylbenzoate Esters: Synthesis and Application to Photoaffinity Labeling of Yeast Protein Farnesyltransferase", <u>J. Org. Chem.</u> , Vol. 61, No. 22,(1996),pp. 7738-7745	
		GIBBS, R A., et al., "A Pd(0)-Catalyzed Route to 13-Methylidenefarnesyl Diphosphate", <u>Tetrahedron Letters</u> , Vol. 35, No. 16,(1994),pp. 2509-2512	
		GIBBS, B S., et al., "Novel Farnesol and Geranylgeranoil Analogues: A Potential New Class of Anticancer Agents Directed against Protein Prenylation", <u>J. Med. Chem.</u> , Vol. 42,(1999),pp. 3800-3808	
		GORENSTEIN, D G., "Stereochemical Effects in Biomolecules", <u>Chem Rev.</u> , Vol. 87, No. 5,(1987),pp. 1047-1077	

EXAMINER

DATE CONSIDERED

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	Unknown
Filing Date	Even Date Herewith
First Named Inventor	Wiemer, David
Group Art Unit	Unknown
Examiner Name	Unknown

Sheet 3 of 5

Attorney Docket No: 875.050US2

	HARTWIG, J F., et al., "Synthesis and DNA-Binding Properties of a Cisplatin Analogue Containing a Tethered Dansyl Group", <u>J. Am. chem. Soc.</u> , Vol. 114,(1992),pp. 8292-8293	
	HENRY, K J., et al., "Discovery of a Series of Cyclohexylethylamine-Containing Protein Farnesyltransferase Inhibitors Exhibiting Potent Cellular Activity", <u>J. Med. Chem.</u> , Vol. 42, No. 23,(1999),pp. 4844-4852	
	HOHL, R J., "Inhibition of Hydroxymethylglutaryl Coenzyme A Reductase Activity Induces a Paradoxical Increase in DNA Synthesis in Myeloid Leukemia Cells", <u>Blood</u> , Vol. 77, No. 5,(March 1, 1991),pp. 1064-1070	
	HOHL, R J., et al., "Stereochemistry-Dependent Inhibition of RAS Farnesylation by Farnesyl Phosphonic Acids", <u>Lipids</u> , Vol. 33, No. 1,(1998),pp. 39-46	
	HOLSTEIN, S A., et al., "Phosphonate and Bisphosphonate Analogues of Farnesyl Pyrophosphate as Potential Inhibitors of Farnesyl Protein Transferase", <u>Bioinorganic & Medicinal Chemistry</u> , Vol. 6,(1998),pp. 687-694	
	HUNT, J T., et al., "Discovery of (R)-7-Cyano-2,3,5,5-tetrahydro-1(1H-imidazol-4-ylmethyl)-3-(phenylmethyl)-4-(2-thienylsulfonyl)-1H-1, 4-benzodiazepine (BMS-214662), a Farnesyltransferase Inhibitor with Potent Preclinical Antitumor Activity", <u>Journal of Medicinal Chemistry</u> , Vol. 43, No. 20,(October 5, 2000),pp. 3587-3595	
	JIANG, K , et al., "The Phosphoinositide 3-OH Kinase/AKT2 Pathway as a Critical Target for Farnesyltransferase Inhibitor-Induced Apoptosis", <u>Molecular and Cellular Biology</u> , Vol. 20, No. 1,(January, 2000),pp. 139-148	
	KANG, M S., et al., "Farnesyl-Derived Inhibitors of Ras Farnesyl Transferase", <u>Biochemical and Biophysical Research Communications</u> , Vol. 217, No. 1,(1995),pp. 245-249	
	KARP, J E., et al., "Clinical and biologic activity of the farnesyltransferase inhibitor R115777 in adults with refractory and relapsed acute leukemias: a phase1 clinical-laboratory correlative trial", <u>Blood</u> , Vol. 97, No. 11,(June 1, 2001),pp. 3361-3369	
	LIU, AI-XUE , et al., "RhoB Alteration Is necessary for Apoptotic and Antineoplastic Responses to Farnesyltransferase Inhibitors", <u>Molecular and Cellular Biology</u> , Vol. 20, No. 16,(August 2000),pp. 6105-6113	
	LONG, S B., et al., "cocrystal Structure of Protein Farnesyltransferase Complexed with Farnesyl Diphosphate Substrate", <u>Biochemistry</u> , Vol. 37,(1998),pp. 9612-9618	
	LUCKMAN, S P., et al., "Nitrogen-containing Bisphosphonated Inhibit the Mevalonate Pathway and Prevent Post-Translational Prenylation of GTP-Binding Proteins, Including Ras", <u>Journal of Bone and Mineral Research</u> , Vol. 13, No. 4,(1998),pp. 581-589	
	MCCLARD, R W., et al., "Novel Phosphonylphosphinyl (P-C-P-C-) Analogues of Biochemically Interesting Diphosphates. Syntheses and Properties of P-C-P-C- Analogues of Isopentenyl Diphosphate and Dimethylallyl Diphosphate", <u>J. Am. Chem. Soc.</u> , Vol. 109,(1987),pp. 5544-5545	

EXAMINER**DATE CONSIDERED**

Substitute Disclosure Statement Form (PTO-1449)

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number Unknown

Filing Date Even Date Herewith

First Named Inventor Wiemer, David

Group Art Unit Unknown

Examiner Name Unknown

Sheet 4 of 5

Attorney Docket No: 875.050US2

		MECHELKE, M F., et al., "Preparation of (2E,6E)-10,11-Dihydrofarnesol via a (Bisphenyl)dithioacetal Reduction", <u>Tetrahedron Letters</u> , Vol. 39,(1998),pp. 9609-9612	
		MECHELKE, M F., et al., "Synthesis of Farnesol Analogues through Cu(I)-Mediated Displacements of Allylic THP Ethers by Grignard Reagents", <u>J. Org. Chem.</u> , Vol. 64, No. 13,(1999),pp. 4821-4829	
		MOASSER, M M., et al., "Farnesyl transferase inhibitors cause enhanced mitotic sensitivity to taxol and epothilones", <u>Proc. Natl. Acad. Sci. USA</u> , Vol. 95,(February, 1998),pp. 1369-1374	
		MU, Y , "Cuprate-Mediated Synthesis and Biological Evaluation of Cyclopropyl- and tert-Butylfarnesyl Diphosphate Analogs", <u>J. Org. Chem.</u> , Vol. 61,(1996),pp. 8010-8015	
		MU, Y. , et al., "On the Stereochemical Course of Human Protein-Farnesyl Transferase", <u>Jouran of the American Chemical Society</u> , Vol. 118, No. 8,(February 28, 1996),pp. 1817-1823	
		OWEN, D J., et al., "Chemo-Enzymatic Synthesis of Fluorescent Rab 7 Proteins: Tools to Study Vesicular Trafficking in Cells", <u>Angew. Chem. Int. Ed.</u> , Vol. 38, No. 4,(1999),pp. 509-512	
		PATEL, D V., et al., "Farnesyl Diphosphate-Based Inhibitors of Ras Farnesyl Protein Transferase", <u>J. Med. Chem.</u> , Vol. 38,(1995),pp. 2906-2921	
		POMPLIANO, D L., et al., "Intramolecular Fluorescence Enhancement: A Continuous Assay of Ras Farnesyl:Protein Transferase", <u>J. Am. Chem. Soc.</u> , Vol. 114,(1992),pp. 7945-7946	
		POMPLIANO, D L., "Steady-State Kinetic Mechanism of Ras Farnesyl:Protein Transferase", <u>Biochemistry</u> , Vol. 31, No. 15,(1992),pp. 3800-3807	
		ROY, MARIE-ODILE , "Mutational and Biochemical Analysis of Plasma Membrane Targeting Mediated by the Farnesylated, Polybasic Carboxy Terminus of K-ras4B", <u>Biochemistry</u> , Vol. 39,(2000),pp. 8298-8307	
		SEPP-LORENZINO, L , et al., "A Peptidomimetic Inhibitor of Farnesyl:Protein Transferase Blocks the Anchorage-dependent and -independent Growth of Human Tumor Cell Lines", <u>Cancer Research</u> , Vol. 55,(November 15, 1995),pp. 5302-5309	
		SUN, J , et al., "Antitumor Efficacy of a Novel Class of Non-thiol-containing Peptidomimetic Inhibitors of Farnesyltransferase and Geranylgeranyltransferase I: Combination Therapy with the Cytotoxic Agents Cisplatin, Taxol, and Gemcitabine", <u>Cancer Research</u> , Vol. 59,(October 1, 1999),pp. 4919-4926	
		TAHIR, S K., et al., "Inhibition of farnesyltransferase with A-176120, a novel and potent farnesyl pyrophosphate analogue", <u>European Journal of Cancer</u> , Vol. 36,(2000),pp. 1161-1170	
		THURMOND, D C., et al., "Regulation of Insulin-stimulated GLUT4 Translocation by Munc18c in 3T3L1 Adipocytes", <u>The Journal of Biological Chemistry</u> , Vol. 273, No. 50,(1998),pp. 33876-33883	
		VALENTIJN, A.R.P.M. , et al., "Synthesis of Pyrophosphonic Acid Analogues of Farnesyl Pyrophosphate", <u>Tetrahedron</u> , Vol. 51, No. 7,(1995),pp. 2099-2108	

EXAMINER

DATE CONSIDERED

Substitute Disclosure Statement Form (PTO-1449)

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is attached

Substitute for form 1449A/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>	<i>Complete if Known</i>	
	Application Number	Unknown
	Filing Date	Even Date Herewith
	First Named Inventor	Wiemer, David
	Group Art Unit	Unknown
	Examiner Name	Unknown
Sheet 5 of 5	Attorney Docket No: 875.050US2	

		VAN BEEK, E , et al., "Farnesyl Pyrophosphate Synthase Is the Molecular Target of Nitrogen-Containing Bisphosphonates", <u>Biochemical and Biophysical research Communications</u> , Vol. 264, No. 1,(1999),pp. 108-111	
		YAMAMOTO, Y , et al., "The Dansyl Group as a Molecular Probe for the Histochemical Localization of a Synthetic Fibronectin-related Peptide", <u>Chemistry Letters</u> , (1994),pp. 1379-1382	
		ZAHN, T J., "Evaluation of Isoprenoid Conformation in Solution and in the Active Site of Protein-Farnesyl Transferase using Carbon-13 Labeling in Conjunction with Solution- and Solid-State NMR", <u>Journal of American Chemical Society</u> , Vol. 122, No. 30,(August 2, 2000),pp. 7153-7164	
		ZAHN, T J., et al., "Synthesis and Conformational Analysis of Di-13C-Labeled Farnesyl Diphosphate Analogs", <u>Tetrahedron Letters</u> , Vol. 39,(1998),pp. 3991-3994	
		ZUJEWSKI, J , et al., "Phase I and Pharmacokinetic Study of Farnesyl Protein Transferase Inhibitor R115777 in Advance Cancer", <u>Journal of Clinical Oncology</u> , Vol. 18, No. 4,(February, 2000),pp. 927-941	

EXAMINER

DATE CONSIDERED